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<110> Ambrose, Helen Jean
      March, Ruth

<120> USE OF POLYMORPHISMS IN HUMAN OATP-C ASSOCIATED WITH AN EFFECT ON STATIN PHARMACOKINETICS IN HUMANS IN STATIN THERAPY

<130> 06275-492US1

<150> PCT/GB2004/003236
<151> 2004-07-26

<150> GB 0317592.4
<151> 2003-07-26

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<170> PatentIn version 3.1

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Ala Leu Ser Leu Ser Phe Ile Ala Lys Thr Leu Gly Ala Ile Ile Met
            35   40   45

Lys Ser Ser Ile Ile His Ile Glu Arg Arg Phe Glu Ile Ser Ser Ser
    50   55   60

Leu Val Gly Phe Ile Asp Gly Ser Phe Glu Ile Gly Asn Leu Leu Val
65   70   75   80

Ile Val Phe Val Ser Tyr Phe Gly Ser Lys Leu His Arg Pro Lys Leu
                85   90   95

Ile Gly Ile Gly Cys Phe Ile Met Gly Ile Gly Gly Val Leu Thr Ala
            100   105   110

Leu Pro His Phe Phe Met Gly Tyr Tyr Arg Tyr Ser Lys Glu Thr Asn
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Ile Asn Ser Ser Glu Asn Ser Thr Ser Thr Leu Ser Thr Cys Leu Ile
    130   135   140

Asn Gln Ile Leu Ser Leu Asn Arg Ala Ser Pro Glu Ile Val Gly Lys
145   150   155   160

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Gly Cys Leu Lys Glu Ser Gly Ser Tyr Met Trp Ile Tyr Val Phe Met
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Gly Asn Met Leu Arg Gly Ile Gly Glu Thr Pro Ile Val Pro Leu Gly
            180             185             190

Leu Ser Tyr Ile Asp Asp Phe Ala Lys Glu Gly His Ser Ser Leu Tyr
            195             200             205

Leu Gly Ile Leu Asn Ala Ile Ala Met Ile Gly Pro Ile Ile Gly Phe
210             215             220

Thr Leu Gly Ser Leu Phe Ser Lys Met Tyr Val Asp Ile Gly Tyr Val
225             230             235             240

Asp Leu Ser Thr Ile Arg Ile Thr Pro Thr Asp Ser Arg Trp Val Gly
            245             250             255

Ala Trp Trp Leu Asn Phe Leu Val Ser Gly Leu Phe Ser Ile Ile Ser
            260             265             270

Ser Ile Pro Phe Phe Phe Leu Pro Gln Thr Pro Asn Lys Pro Gln Lys
            275             280             285

Glu Arg Lys Ala Ser Leu Ser Leu His Val Leu Glu Thr Asn Asp Glu
    290             295             300

Lys Asp Gln Thr Ala Asn Leu Thr Asn Gln Gly Lys Asn Ile Thr Lys
305             310             315             320

Asn Val Thr Gly Phe Phe Gln Ser Phe Lys Ser Ile Leu Thr Asn Pro
            325             330             335

Leu Tyr Val Met Phe Val Leu Leu Thr Leu Leu Gln Val Ser Ser Tyr
            340             345             350

Ile Gly Ala Phe Thr Tyr Val Phe Lys Tyr Val Glu Gln Gln Tyr Gly
            355             360             365

Gln Pro Ser Ser Lys Ala Asn Ile Leu Leu Gly Val Ile Thr Ile Pro
    370             375             380

Ile Phe Ala Ser Gly Met Phe Leu Gly Gly Tyr Ile Ile Lys Lys Phe
385             390             395             400

Lys Leu Asn Thr Val Gly Ile Ala Lys Phe Ser Cys Phe Thr Ala Val
            405             410             415

Met Ser Leu Ser Phe Tyr Leu Leu Tyr Phe Phe Ile Leu Cys Glu Asn
            420             425             430
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Lys Ser Val Ala Gly Leu Thr Met Thr Tyr Asp Gly Asn Asn Pro Val
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Thr Ser His Arg Asp Val Pro Leu Ser Tyr Cys Asn Ser Asp Cys Asn
    450                 455             460

Cys Asp Glu Ser Gln Trp Glu Pro Val Cys Gly Asn Asn Gly Ile Thr
465             470             475                 480

Tyr Ile Ser Pro Cys Leu Ala Gly Cys Lys Ser Ser Ser Gly Asn Lys
            485             490                 495

Lys Pro Ile Val Phe Tyr Asn Cys Ser Cys Leu Glu Val Thr Gly Leu
            500             505             510

Gln Asn Arg Asn Tyr Ser Ala His Leu Gly Glu Cys Pro Arg Asp Asp
        515             520             525

Ala Cys Thr Arg Lys Phe Tyr Phe Phe Val Ala Ile Gln Val Leu Asn
    530             535             540

Leu Phe Phe Ser Ala Leu Gly Gly Thr Ser His Val Met Leu Ile Val
545             550             555             560

Lys Ile Val Gln Pro Glu Leu Lys Ser Leu Ala Leu Gly Phe His Ser
            565             570             575

Met Val Ile Arg Ala Leu Gly Gly Ile Leu Ala Pro Ile Tyr Phe Gly
            580             585             590

Ala Leu Ile Asp Thr Thr Cys Ile Lys Trp Ser Thr Asn Asn Cys Gly
    595             600             605

Thr Arg Gly Ser Cys Arg Thr Tyr Asn Ser Thr Ser Phe Ser Arg Val
    610             615             620

Tyr Leu Gly Leu Ser Ser Met Leu Arg Val Ser Ser Leu Val Leu Tyr
625             630             635             640

Ile Ile Leu Ile Tyr Ala Met Lys Lys Tyr Gln Glu Lys Asp Ile
            645             650             655

Asn Ala Ser Glu Asn Gly Ser Val Met Asp Glu Ala Asn Leu Glu Ser
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Ala Leu Ser Leu Ser Phe Ile Ala Lys Thr Leu Gly Ala Ile Ile Met
        35   40   45

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Lys Ser Ser Ile Ile His Ile Glu Arg Arg Phe Glu Ile Ser Ser Ser
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Leu Val Gly Phe Ile Asp Gly Ser Phe Glu Ile Gly Asn Leu Leu Val
65              70                  75                  80

Ile Val Phe Val Ser Tyr Phe Gly Ser Lys Leu His Arg Pro Lys Leu
                85              90                  95

Ile Gly Ile Gly Cys Phe Ile Met Gly Ile Gly Gly Val Leu Thr Ala
            100             105             110

Leu Pro His Phe Phe Met Gly Tyr Tyr Arg Tyr Ser Lys Glu Thr Asn
            115             120             125

Ile Asp Ser Ser Glu Asn Ser Thr Ser Thr Leu Ser Thr Cys Leu Ile
    130             135             140

Asn Gln Ile Leu Ser Leu Asn Arg Ala Ser Pro Glu Ile Val Gly Lys
145             150             155             160

Gly Cys Leu Lys Glu Ser Gly Ser Tyr Met Trp Ile Tyr Ala Phe Met
            165             170             175

Gly Asn Met Leu Arg Gly Ile Gly Glu Thr Pro Ile Val Pro Leu Gly
            180             185             190

Leu Ser Tyr Ile Asp Asp Phe Ala Lys Glu Gly His Ser Ser Leu Tyr
        195             200             205

Leu Gly Ile Leu Asn Ala Ile Ala Met Ile Gly Pro Ile Ile Gly Phe
    210             215             220

Thr Leu Gly Ser Leu Phe Ser Lys Met Tyr Val Asp Ile Gly Tyr Val
225             230             235             240

Asp Leu Ser Thr Ile Arg Ile Thr Pro Thr Asp Ser Arg Trp Val Gly
            245             250             255

Ala Trp Trp Leu Asn Phe Leu Val Ser Gly Leu Phe Ser Ile Ile Ser
            260             265             270

Ser Ile Pro Phe Phe Phe Leu Pro Gln Thr Pro Asn Lys Pro Gln Lys
        275             280             285

Glu Arg Lys Ala Ser Leu Ser Leu His Val Leu Glu Thr Asn Asp Glu
    290             295             300

Lys Asp Gln Thr Ala Asn Leu Thr Asn Gln Gly Lys Asn Ile Thr Lys
305             310             315             320
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Asn Val Thr Gly Phe Phe Gln Ser Phe Lys Ser Ile Leu Thr Asn Pro
            325             330             335

Leu Tyr Val Met Phe Val Leu Leu Thr Leu Leu Gln Val Ser Ser Tyr
            340             345             350

Ile Gly Ala Phe Thr Tyr Val Phe Lys Tyr Val Glu Gln Gln Tyr Gly
            355             360             365

Gln Pro Ser Ser Lys Ala Asn Ile Leu Leu Gly Val Ile Thr Ile Pro
    370             375             380

Ile Phe Ala Ser Gly Met Phe Leu Gly Gly Tyr Ile Ile Lys Lys Phe
385             390             395             400

Lys Leu Asn Thr Val Gly Ile Ala Lys Phe Ser Cys Phe Thr Ala Val
            405             410             415

Met Ser Leu Ser Phe Tyr Leu Leu Tyr Phe Phe Ile Leu Cys Glu Asn
            420             425             430

Lys Ser Val Ala Gly Leu Thr Met Thr Tyr Asp Gly Asn Asn Pro Val
            435             440             445

Thr Ser His Arg Asp Val Pro Leu Ser Tyr Cys Asn Ser Asp Cys Asn
    450             455             460

Cys Asp Glu Ser Gln Trp Glu Pro Val Cys Gly Asn Asn Gly Ile Thr
465             470             475             480

Tyr Ile Ser Pro Cys Leu Ala Gly Cys Lys Ser Ser Ser Gly Asn Lys
            485             490             495

Lys Pro Ile Val Phe Tyr Asn Cys Ser Cys Leu Glu Val Thr Gly Leu
            500             505             510

Gln Asn Arg Asn Tyr Ser Ala His Leu Gly Glu Cys Pro Arg Asp Asp
    515             520             525

Ala Cys Thr Arg Lys Phe Tyr Phe Phe Val Ala Ile Gln Val Leu Asn
    530             535             540

Leu Phe Phe Ser Ala Leu Gly Gly Thr Ser His Val Met Leu Ile Val
545             550             555             560

Lys Ile Val Gln Pro Glu Leu Lys Ser Leu Ala Leu Gly Phe His Ser
            565             570             575

Met Val Ile Arg Ala Leu Gly Gly Ile Leu Ala Pro Ile Tyr Phe Gly
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              580                    585    :              590

Ala Leu Ile Asp Thr Thr Cys Ile Lys Trp Ser Thr Asn Asn Cys Gly
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Thr Arg Gly Ser Cys Arg Thr Tyr Asn Ser Thr Ser Phe Ser Arg Val
    610             615             620

Tyr Leu Gly Leu Ser Ser Met Leu Arg Val Ser Ser Leu Val Leu Tyr
625             630             635             640

Ile Ile Leu Ile Tyr Ala Met Lys Lys Lys Tyr Gln Glu Lys Asp Ile
            645             650             655

Asn Ala Ser Glu Asn Gly Ser Val Met Asp Glu Ala Asn Leu Glu Ser
            660             665             670

Leu Asn Lys Asn Lys His Phe Val Pro Ser Ala Gly Ala Asp Ser Glu
        675             680             685

Thr His Cys
    690


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Met Asp Gln Asn Gln His Leu Asn Lys Thr Ala Glu Ala Gln Pro Ser
1               5               10              15

Glu Asn Lys Lys Thr Arg Tyr Cys Asn Gly Leu Lys Met Phe Leu Ala
            20              25              30

Ala Leu Ser Leu Ser Phe Ile Ala Lys Thr Leu Gly Ala Ile Ile Met
    35              40              45

Lys Ser Ser Ile Ile His Ile Glu Arg Arg Phe Glu Ile Ser Ser Ser
    50              55              60

Leu Val Gly Phe Ile Asp Gly Ser Phe Glu Ile Gly Asn Leu Leu Val
65              70              75              80

Ile Val Phe Val Ser Tyr Phe Gly Ser Lys Leu His Arg Pro Lys Leu
            85              90              95

Ile Gly Ile Gly Cys Phe Ile Met Gly Ile Gly Gly Val Leu Thr Ala
            100             105             110

Leu Pro His Phe Phe Met Gly Tyr Tyr Arg Tyr Ser Lys Glu Thr Asn
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            115                 120                 125

Ile Asn Ser Ser Glu Asn Ser Thr Ser Thr Leu Ser Thr Cys Leu Ile
    130                 135                 140

Asn Gln Ile Leu Ser Leu Asn Arg Ala Ser Pro Glu Ile Val Gly Lys
145                 150                 155                 160

Gly Cys Leu Lys Glu Ser Gly Ser Tyr Met Trp Ile Tyr Ala Phe Met
                165                 170                 175

Gly Asn Met Leu Arg Gly Ile Gly Glu Thr Pro Ile Val Pro Leu Gly
            180                 185                 190

Leu Ser Tyr Ile Asp Asp Phe Ala Lys Glu Gly His Ser Ser Leu Tyr
            195                 200                 205

Leu Gly Ile Leu Asn Ala Ile Ala Met Ile Gly Pro Ile Ile Gly Phe
    210                 215                 220

Thr Leu Gly Ser Leu Phe Ser Lys Met Tyr Val Asp Ile Gly Tyr Val
225                 230                 235                 240

Asp Leu Ser Thr Ile Arg Ile Thr Pro Thr Asp Ser Arg Trp Val Gly
                245                 250                 255

Ala Trp Trp Leu Asn Phe Leu Val Ser Gly Leu Phe Ser Ile Ile Ser
            260                 265                 270

Ser Ile Pro Phe Phe Phe Leu Pro Gln Thr Pro Asn Lys Pro Gln Lys
        275                 280                 285

Glu Arg Lys Ala Ser Leu Ser Leu His Val Leu Glu Thr Asn Asp Glu
    290                 295                 300

Lys Asp Gln Thr Ala Asn Leu Thr Asn Gln Gly Lys Asn Ile Thr Lys
305                 310                 315                 320

Asn Val Thr Gly Phe Phe Gln Ser Phe Lys Ser Ile Leu Thr Asn Pro
                325                 330                 335

Leu Tyr Val Met Phe Val Leu Leu Thr Leu Leu Gln Val Ser Ser Tyr
            340                 345                 350

Ile Gly Ala Phe Thr Tyr Val Phe Lys Tyr Val Glu Gln Gln Tyr Gly
        355                 360                 365

Gln Pro Ser Ser Lys Ala Asn Ile Leu Leu Gly Val Ile Thr Ile Pro
    370                 375                 380
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Ile Phe Ala Ser Gly Met Phe Leu Gly Gly Tyr Ile Ile Lys Lys Phe
385             390             395             400

Lys Leu Asn Thr Val Gly Ile Ala Lys Phe Ser Cys Phe Thr Ala Val
                405             410             415

Met Ser Leu Ser Phe Tyr Leu Leu Tyr Phe Phe Ile Leu Cys Glu Asn
            420             425             430

Lys Ser Val Ala Gly Leu Thr Met Thr Tyr Asp Gly Asn Asn Pro Val
        435             440             445

Thr Ser His Arg Asp Val Pro Leu Ser Tyr Cys Asn Ser Asp Cys Asn
    450             455             460

Cys Asp Glu Ser Gln Trp Glu Pro Val Cys Gly Asn Asn Gly Ile Thr
465             470             475             480

Tyr Ile Ser Pro Cys Leu Ala Gly Cys Lys Ser Ser Ser Gly Asn Lys
            485             490             495

Lys Pro Ile Val Phe Tyr Asn Cys Ser Cys Leu Glu Val Thr Gly Leu
            500             505             510

Gln Asn Arg Asn Tyr Ser Ala His Leu Gly Glu Cys Pro Arg Asp Asp
        515             520             525

Ala Cys Thr Arg Lys Phe Tyr Phe Phe Val Ala Ile Gln Val Leu Asn
    530             535             540

Leu Phe Phe Ser Ala Leu Gly Gly Thr Ser His Val Met Leu Ile Val
545             550             555             560

Lys Ile Val Gln Pro Glu Leu Lys Ser Leu Ala Leu Gly Phe His Ser
            565             570             575

Met Val Ile Arg Ala Leu Gly Gly Ile Leu Ala Pro Ile Tyr Phe Gly
            580             585             590

Ala Leu Ile Asp Thr Thr Cys Ile Lys Trp Ser Thr Asn Asn Cys Gly
        595             600             605

Thr Arg Gly Ser Cys Arg Thr Tyr Asn Ser Thr Ser Phe Ser Arg Val
    610             615             620

Tyr Leu Gly Leu Ser Ser Met Leu Arg Val Ser Ser Leu Val Leu Tyr
625             630             635             640

Ile Ile Leu Ile Tyr Ala Met Lys Lys Tyr Gln Glu Lys Asp Ile
            645             650             655
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-12-

Asn Ala Ser Glu Asn Gly Ser Val Met Asp Glu Ala Asn Leu Glu Ser
            660   665   670

Leu Asn Lys Asn Lys His Phe Val Pro Ser Ala Gly Ala Asp Ser Glu
        675   680   685

Thr His Cys
    690